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PRINCIPAL INVESTIGATOR: David R King, MD

CONTRACTING ORGANIZATION: Massachusetts General Hospital
Boston, MA 02114

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David R King, MD

E-Mail:

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Massachusetts General Hospital
55 Fruit Street
Boston, MA 02114

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14. ABSTRACT

The purpose of the study was to evaluate real-time heart rate complexity as a trauma triage tool. Objectives achieved include

1. Real-time complexity determination has been demonstrated in trauma activation patients.
2. The real-time measures have been miniaturized into a hand-held device that is portable and user friendly
3. Triage algorithms have been proposed based upon prospectively collected data on trauma patients presenting to our institution.
4. The algorithm has been tested prospectively and retrospectively

Key findings include:

Heart rate complexity can be miniaturized and conducted in real time.

Real-time analysis with a hand-held device is possible and results in improved trauma patient triage over standard existing triage guidelines.

Adding electrical cardiometry to HRC-based triage does not improve triage

HRC-based triage is valid after a variety of mechanisms of injury, including bunt, penetrating, and blast trauma.

15. SUBJECT TERMS
Complexity, variability, trauma, triage

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Table of Contents

Introduction

The objective of this study is to prospectively evaluate novel multiscale measures of heart-rate variability, complexity and entropy in a traumatized population undergoing evaluation, resuscitation, and definitive treatment. We hypothesize that HRVC will discriminate patients who require rapid escalation of care from those who are relatively uninjured. Our long term goal is to develop a new objective vital sign that can be used as a trauma triage tool on the battlefield. To test this hypothesis, we will examine heart-rate variability, complexity and entropy in trauma patients presenting to our Level One trauma center and correlate those findings with standard vital signs, interventions, and outcomes. We have proposed the following specific aims to test this hypothesis and achieve our goal.

1. Demonstrate feasibility of real-time HRVC and electrical cardiometry analysis in trauma patients
2. Characterize HRVC and electrical cardiometry changes during trauma evaluation and resuscitation
3. Develop an HRVC and electrical cardiometry-based triage model
4. Retrospectively apply the developed model to all prospectively evaluated patients

Body

PROJECT RESULTS:

All objectives were achieved despite funding withdrawal half way through the study period.

5. Real-time complexity determination has been demonstrated in trauma activation patients.
6. The real-time measures have been miniaturized into a hand-held device that is portable and user friendly
7. Triage algorithms have been proposed based upon prospectively collected data on trauma patients presenting to our institution.
8. The algorithm has been tested prospectively and retrospectively

Attached to this report are several peer-reviewed publications that describe, in detail, the development and testing of this real-time device and it's usefulness in triage, including in patients analyzed after the Boston Marathon bombings.

Key Research Accomplishments

- Heart rate complexity can be miniaturized and conducted in real time.
- Real-time analysis with a hand-held device is possible and results in improved trauma patient triage over standard existing triage guidelines.
- Adding electrical cardiometry to HRC-based triage does not improve triage
- HRC-based triage is valid after a variety of mechanisms of injury, including bunt, penetrating, and blast trauma.

Reportable Outcomes

This funding directly resulted in three peer-reviewed publications and six abstract presentations at local and national meetings.

Conclusions

Real-time heart rate complexity if a useful trauma triage tool and may improve detection of impending life-threatening conditions where standard vital signs do not.

References

None

Appendices

Mejaddam AY, van der Wilden GM, Chang Y, Cropano CM, Sideris AC, Hwabejire JO, Velmahos GC, Alam HB, de Moya MA, King DR. Development of a rugged handheld device for real-time analysis of heart rate: entropy in critically ill patients. J Spec Oper Med. 2013 Spring;13(1):29-33.

Majaddam AY, Birkham OA, Sideris AC, Van Der Wilden GM, Imam AM, Hwabejire JO, Chang Y, Velmahos G, Fagenholz PJ, Yeh DD, deMoya MA, King DR. Real Time Heart Rate Entropy Predicts the Need for Life Saving Interventions in Trauma Activation Patients. J Trauma Acute Care Surg. 2013 Oct;75(4):607-12.

Peev MP, Naraghi L, Chang Y, Velmahos G, King DR. Real Time Heart Rate Entropy Predicts Life Saving Interventions After The Boston Marathon Bombing. J Crit Care. 2013 Oct 10.

Supporting Data

n/a

Development of a Rugged Handheld Device for Real-Time Analysis of Heart Rate: Entropy in Critically Ill Patients

Ali Y. Mejaddam, MD; Gwendolyn M. van der Wilden, MSc; Yuchiao Chang, PhD; Catrina M. Cropano, BSc; Antonis C. Sideris, MD; John O. Hwabejire, MD; George C. Velmahos, MD, PhD; Hasan B. Alam, MD; Marc A. de Moya, MD; David R. King, MD

ABSTRACT

Introduction: The usefulness of heart rate variability (HRV) and heart rate complexity (HRC) analysis as a potential triage tool has been limited by the inability to perform real-time analysis on a portable, handheld monitoring platform. Through a multidisciplinary effort of academia and industry, we report on the development of a rugged, handheld and noninvasive device that provides HRV and HRC analysis in real-time in critically ill patients. **Methods:** After extensive re-engineering, real-time HRV and HRC analyses were incorporated into an existing, rugged, handheld monitoring platform. Following IRB approval, the prototype device was used to monitor 20 critically ill patients and 20 healthy controls to demonstrate real-world discriminatory potential. Patients were compared to healthy controls using a Student's *t* test as well as repeated measures analysis. Receiver operator characteristic (ROC) curves were generated for HRV and HRC. **Results:** Critically ill patients had a mean APACHE-2 score of 15, and over 50% were mechanically ventilated and requiring vasopressor support. HRV and HRC were both lower in the critically ill patients compared to healthy controls ($p < 0.0001$) and remained so after repeated measures analysis. The area under the ROC for HRV and HRC was 0.95 and 0.93, respectively. **Conclusions:** This is the first demonstration of real-time, handheld HRV and HRC analysis. This prototype device successfully discriminates critically ill patients from healthy controls. This may open up possibilities for real-world use as a trauma triage tool, particularly on the battlefield.

KEYWORDS: *heart rate complexity; heart rate variability; entropy; triage; combat*

Introduction

The physiologic adaptive response of the heart to hemorrhage and critical illness is complex and influenced by a multitude of efferent inputs from the within the cardiovascular, respiratory, and neuroendocrine systems.[1,2] Heart rate variability (HRV) relies on the physiologic premise that high variability, or sinoatrial responsiveness, is a sign of neurocardiovascular adaptability, thus implying a healthy state with an appropriate and predictable myocardial response.[1-3] Conversely, low variability indicates an abnormal or inadequate response of the heart, signifying poor sinoatrial responsiveness to stimuli and subsequent morbidity in the affected individual.[2] HRV analysis is increasingly described in the literature as an early indicator of compromised health and a potentially useful trauma triage tool.[4-6] An alternative, and likely more robust, approach to analysis of cardiac sinoatrial variability is quantification of the amount of irregularity in the sinoatrial responsiveness, known as heart rate complexity (HRC).[7,8] A decreased irregularity, or loss of complexity, has been suggested to reflect impaired adaptation to physiologic stress[7,8] and indicates physiologic derangement and injury, under the appropriate clinical circumstances.

Traditional vital signs, such as heart rate (HR) and blood pressure (BP), have significant limitations as trauma triage tools because they integrate compensatory mechanisms that may conceal the true severity of injury until physiologic exhaustion occurs.[6] The overall goal of trauma triage is to identify high-risk injured patients who would benefit from aggressive, resource-intensive medical care (appropriate triage) while limiting exclusion of patients who could benefit from such care (under triage). Today,

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Real-time heart rate entropy predicts the need for lifesaving interventions in trauma activation patients

Ali Y. Mejaddam, MD, Oscar A. Birkhan, MD, Antonis C. Sideris, MD, Gwendolyn M. Van der Wilden, MD, Ayesha M. Imam, MD, John O. Hwabejire, MD, Yuchiao Chang, PhD, George C. Velmahos, MD, PhD, Peter J. Fagenholz, MD, Daniel D. Yeh, MD, Marc A. de Moya, MD, *and* **David Richard King, MD, MC, USAR,** *Boston, Massachusetts*

BACKGROUND: Heart rate complexity (HRC), commonly described as a "new vital sign," has shown promise in predicting injury severity, but its use in clinical practice has been precluded by the absence of real-time data. This study was conducted to evaluate the utility of real-time, automated, instantaneous, hand-held heart rate entropy analysis in predicting the need for lifesaving interventions (LSIs). We hypothesized that real-time HRC would predict LSIs.

METHODS: Prospective enrollment of patients who met criteria for trauma team activation was conducted at a Level I trauma center (September 2011 to February 2012). A novel, hand-held, portable device was used to measure HRC (by sample entropy) and time-domain heart rate variability continuously in real time for 2 hours after the moment of presentation. Electric impedance cardiography was used to determine cardiac output. Patients who received an LSI were compared with patients without any intervention (non-LSI). Multivariable analysis was performed to control for differences between the groups.

RESULTS: Of 82 patients enrolled, 21 (26%) received 67 LSIs within 24 hours of hospital arrival. Initial systolic blood pressure was similar in both groups. LSI patients had a lower Glasgow Coma Scale (GCS) score (9.2 [5.1] vs. 14.9 [0.2], $p < 0.0001$). The mean (SD) HRC value on presentation was 0.8 (0.6) in the LSI group compared with 1.5 (0.6) in the non-LSI group ($p < 0.0001$). With the use of logistic regression, initial HRC was the only significant predictor of LSI. A cutoff value for HRC of 1.1 yields sensitivity, specificity, negative predictive value, and positive predictive value of 86%, 74%, 94%, and 53%, respectively, with an accuracy of 77% for predicting an LSI.

CONCLUSION: Decreased HRC on hospital arrival is an independent predictor of the need for LSI in trauma activation patients. Real-time HRC may be a useful adjunct to standard vital signs monitoring and predicts LSIs. (*J Trauma Acute Care Surg.* 2013;75: 607-612.

LEVEL OF EVIDENCE: Prognostic and diagnostic study, level III.

KEY WORDS: Entropy; combat; triage; complexity; variability.

Traditional vital signs often fail to reflect the true severity of injury in trauma patients until compensatory mechanisms have been exhausted.[1–3] In fact, heart rate (HR) may even decrease in response to severe trauma, which carries a risk of undertriage and, consequently, increased mortality.[4] HR variability (HRV), commonly described as a "new vital sign," has shown promise in predicting injury severity, but its use in clinical practice has been precluded by the absence of real-time data.[4,6–8]

The primary goal of trauma triage is to identify high-risk patients who would benefit from aggressive medical care (appropriate triage) while limiting exclusion of those who could benefit from such care (undertriage).[8] Specificity of cutoff criteria for trauma team activation is often sacrificed for an increased sensitivity. Furthermore, current triage systems are supported by little evidence and commonly reflect expert opinion.[9,10] These limitations are particularly apparent in combat casualty care, in which the need to minimize the risk for medics has led to the concept of "remote triage."[3,11] To achieve this, soldiers would be equipped with sensors that transmit data to the medic. HRV analysis (SD of R-R intervals (RRIs) in the frequency domain) would be a useful remote triage tool as previously reported[2–4,6–8,11–14] if it were available in real-time.

Recent studies using an alternative approach for quantifying cardiac variability, based on the amount of signal irregularity as measured in the RRI times series of the electrocardiogram using the method of entropy, have indicated a superior diagnostic performance to predict poor outcome.[3,4,7] As biologic systems are inherently complex, a decreased RRI irregularity or loss of HR complexity (HRC) has been suggested to reflect impaired adaptation to physiologic stress.[3,4,15]

We have developed and miniaturized a device that allows instantaneous measurement of cardiac variability (HRV and HRC) on a hand-held, portable monitor. To the best of our knowledge, no study has examined the diagnostic utility of real-time HRV and HRC analysis for predicting the need of lifesaving interventions (LSIs) in trauma patients upon hospital arrival. We hypothesized that HRV and HRC are decreased in patients who

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From the Division of Trauma, Emergency Surgery, and Surgical Critical Care, Massachusetts General Hospital and Harvard Medical School, Boston, Massachusetts.

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Address for reprints: LTC David R. King, MD, MC, USAR, Division of Trauma, Emergency Surgery, and Surgical Critical Care, Massachusetts General Hospital and Harvard Medical School, 165 Cambridge St, Suite 810, Boston, MA 02114; email: Dking3@partners.org.

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Electronic Articles

Real-time sample entropy predicts life-saving interventions after the Boston Marathon bombing ☆

Miroslav P. Peev, MD, Leily Naraghi, MD, Yuchiao Chang, PhD, Marc DeMoya, MD, Peter Fagenholz, MD, Daniel Yeh, MD, George Velmahos, MD, PhD, David R. King *

Department of Surgery, Division of Trauma, Emergency Surgery and Surgical Critical Care, Massachusetts General Hospital and Harvard Medical School, Boston, MA 02114, USA

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ABSTRACT

Purpose: Identifying patients in need of a life-saving intervention (LSI) during a mass casualty event is a priority. We hypothesized that real-time, instantaneous sample entropy (SampEn) could predict the need for LSI in the Boston Marathon bombing victims.

Materials and methods: Severely injured Boston Marathon bombing victims (n = 10) had sample entropy (SampEn) recorded upon presentation using a continuous 200-beat rolling average in real time. Treating clinicians were blinded to real-time results. The correlation between SampEn, injury severity, number, and type of LSI was examined.

Results: Victims were males (60%) with a mean age of 39.1 years. Injuries involved lower extremities (50.0%), head and neck (24.2%), or upper extremities (9.7%). Sample entropy negatively correlated with Injury Severity Score ($r = -0.70$; $P = .023$), number of injuries ($r = -0.70$; $P = .026$), and the number and need for LSI ($r = -0.82$; $P = .004$). Sample entropy was reduced under a variety of conditions.

	SampEn (mean ± SD)	*P*
Amputation, n = 5	0.7 ± 0.3	
No amputation, n = 5	1.9 ± 0.8	.027
Transfusion, n = 5	0.7 ± 0.3	
No transfusion, n = 5	1.9 ± 0.8	.027
Intubation, n = 6	0.8 ± 0.3	
No intubation, n = 4	2.1 ± 0.7	.027
Vasopressors, n = 7	0.8 ± 0.3	
No vasopressors, n = 3	2.4 ± 0.3	.004

Conclusions: Sample entropy strongly correlates with injury severity and predicts LSI after blast injuries sustained in the Boston Marathon bombings. Sample entropy may be a useful triage tool after blast injury.

1. Background

Appropriate triage of patients after traumatic injury remains a challenge, especially during mass casualty events, such as the Boston Marathon bombing on April 15, 2013. Despite the large number of victims, not all would be severely injured or require life-saving interventions (LSI). Traditional vital signs may not become altered until compensatory physiologic mechanisms become completely exhausted [1]. Various measures of heart rate variability (HRV) and complexity have been shown to be superior to vital signs at predicting mortality after trauma [2,3]. Reduced irregularity or loss of complexity due to traumatic injury has been previously been associated with increased need of prehospital LSI and mortality [1,4]. Of note, these studies have all required prospective data collection with off-line, retrospective data analysis (or manually verified R wave detection), consequently making real-time analysis impossible.

The aim of this study was to prospectively evaluate the use of a real-time measure of heart rate complexity as a potential triage tool during the tragic events of the Boston Marathon bombing. We hypothesized that real-time, instantaneous heart rate complexity could predict the need for LSI in the Boston Marathon bombing victims.

2. Methods

The Massachusetts General Hospital is an academic level 1 trauma center managed by an unchanging dedicated trauma and acute care surgery team. Patients that met criteria for trauma team activation

☆ No authors have any conflicts of interest.

* Corresponding author.
E-mail address: dking3@partners.org (D.R. King).

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